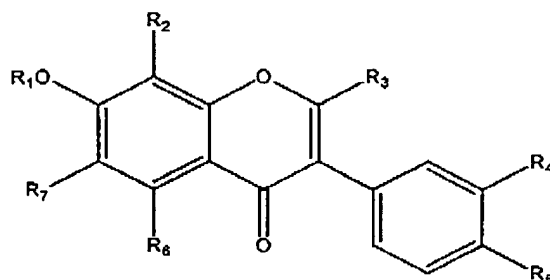


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APPENDIX A

CLEAN COPY OF CLAIMS AS AMENDED HEREIN

1. A method for inhibiting ALDH-2 comprising contacting ALDH-2 with a compound of Formula I



Formula I

wherein:

R₁ is selected from the group consisting of hydrogen, carboxy, halo, branched or straight chain (C₁-C₆)haloalkyl, (C₃-C₆)cycloalkoxy, (C₁-C₆)haloalkoxy, (C₃-C₆)cyclohaloalkoxy, (C₃-C₆)cycloalkoxyalkyl, (C₁-C₆)alkoxy(C₃-C₆)cycloalkyl, (C₃-C₆)cycloalkylcarbonyl, substituted or unsubstituted phenyl, phenyl(C₁-C₆)alkyl, and heterocyclyloxy, heterocyclylcarbonyl, wherein substituents are from one to four and are selected from the group consisting of halo, aminocarbonyl, aminothiocarbonyl, carboxy, formyl, hydroxy, amino, carbamoyl, (C₁-C₃)alkyl, (C₁-C₃)haloalkyl, (C₁-C₃)alkoxy, (C₁-C₃)haloalkoxy, (C₁-C₃)alkylamino, di(C₁-C₃)alkylamino, (C₁-C₂)alkoxy(C₁-C₂)alkyl, (C₁-C₂)alkylamino(C₁-C₂)alkyl, di(C₁-C₂)alkylamino(C₁-C₂)alkyl, (C₁-C₃)alkylcarbonyl, (C₁-C₃)alkoxycarbonyl, (C₁-C₃)alkylaminocarbonyl, and di (C₁-C₃)alkylaminocarbonyl;

R₂ is selected from the group consisting of hydrogen and alkoxy;

R₃ is selected from the group consisting of hydrogen, C₁-C₆ alkoxycarbonyl, carboxy and sugar;

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R₄ is selected from the group consisting of hydrogen and hydroxy;

R₅ is selected from the group consisting of hydrogen, carboxy, hydroxy, amino, halo, branched or straight chain (C₁-C₆)alkyl, (C₁-C₆)haloalkyl, (C₂-C₆)alkenyl, (C₃-C₆)alkadienyl, (C₁-C₆)alkoxy, (C₃-C₆)cycloalkoxy, (C₁-C₆)haloalkoxy, (C₃-C₆)cyclohaloalkoxy, (C₂-C₆)alkynyloxy, (C₁-C₆)alkoxy(C₁-C₆)alkyl, (C₃-C₆)cycloalkoxyalkyl, (C₁-C₆)alkoxy(C₃-C₆)cycloalkyl, (C₁-C₆)alkylcarbonyl, (C₃-C₆)cycloalkylcarbonyl, (C₁-C₆)alkoxycarbonyl, (C₄-C₆)alkoxycarbonylalkyl, (C₁-C₆)hydroxyalkyl, substituted or unsubstituted phenyl, phenyl(C₁-C₆)alkyl, heterocyclyl, heterocyclyloxy, heterocyclylcarbonyl, wherein substituents are from one to four and are selected from the group consisting of halo, aminocarbonyl, aminothiocarbonyl, carboxy, formyl, hydroxy, amino, carbamoyl, (C₁-C₃)alkyl, (C₁-C₃)haloalkyl, (C₁-C₃)alkoxy, (C₁-C₃)haloalkoxy, (C₁-C₃)alkylamino, di(C₁-C₃)alkylamino, (C₁-C₂)alkoxy(C₁-C₂)alkyl, (C₁-C₂)alkylamino(C₁-C₂)alkyl, di(C₁-C₂)alkylamino(C₁-C₂)alkyl, (C₁-C₃)alkylcarbonyl, (C₁-C₃)alkoxycarbonyl, (C₁-C₃)alkylaminocarbonyl, and di (C₁-C₃)alkylaminocarbonyl;

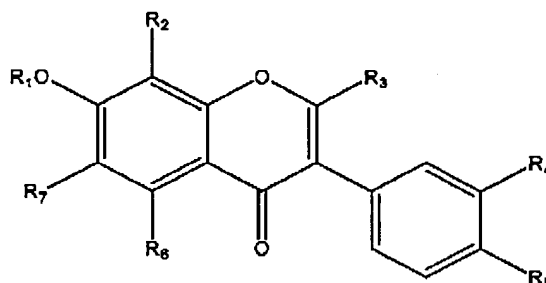
R₆ is selected from the group consisting of hydrogen and hydroxy, and

R₇ is selected from the group consisting of hydrogen and halogen

with the proviso that R₅ cannot be hydroxy when R₁, R₂, R₃, R₄, R₆, and R₇ are all hydrogen.

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2. A method for inhibiting ALDH-2 comprising contacting ALDH-2 with a compound of Formula I



Formula I

wherein:

R₁ is selected from the group consisting of hydrogen, carboxy, halo, branched or straight chain (C₁-C₆)alkyl, (C₁-C₆)haloalkyl, (C₂-C₆)alkenyl, (C₃-C₆)alkadienyl, (C₁-C₆)alkoxy, (C₃-C₆)cycloalkoxy, (C₁-C₆)haloalkoxy, (C₃-C₆)cyclohaloalkoxy, (C₂-C₆)alkynyloxy, (C₁-C₆)alkoxy(C₁-C₆)alkyl, (C₃-C₆)cycloalkoxyalkyl, (C₁-C₆)alkoxy(C₃-C₆)cycloalkyl, (C₁-C₆)alkylcarbonyl, (C₃-C₆)cycloalkylcarbonyl, (C₁-C₆)alkoxycarbonyl, (C₄-C₆)alkoxycarbonylalkyl, (C₁-C₆)hydroxyalkyl, (C₅-C₁₀)carboxyalkyl, substituted or unsubstituted phenyl, phenyl(C₁-C₆)alkyl, heterocyclyl, heterocyclyloxy, heterocyclylcarbonyl, wherein substituents are from one to four and are selected from the group consisting of halo, aminocarbonyl, aminothiocarbonyl, carboxy, formyl, hydroxy, amino, carbamoyl, (C₁-C₃)alkyl, (C₁-C₃)haloalkyl, (C₁-C₃)alkoxy, (C₁-C₃)haloalkoxy, (C₁-C₃)alkylamino, di(C₁-C₃)alkylamino, (C₁-C₂)alkoxy(C₁-C₂)alkyl, (C₁-C₂)alkylamino(C₁-C₂)alkyl, di(C₁-C₂)alkylamino(C₁-C₂)alkyl, (C₁-C₃)alkylcarbonyl, (C₁-C₃)alkoxycarbonyl, (C₁-C₃)alkylaminocarbonyl, and di (C₁-C₃)alkylaminocarbonyl;

R₂ is selected from the group consisting of hydrogen and alkoxy;

R₃ is selected from the group consisting of hydrogen, C₁-C₆ alkoxycarbonyl, carboxy and sugar;

R₄ is selected from the group consisting of hydrogen and hydroxy;

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R₅ is selected from the group consisting of hydrogen, carboxy, halo, amino, branched or straight chain (C₁-C₆)alkyl, (C₁-C₆)haloalkyl, (C₂-C₆)alkenyl, (C₃-C₆)alkadienyl, (C₁-C₆)alkoxy, (C₃-C₆)cycloalkoxy, (C₁-C₆)haloalkoxy, (C₃-C₆)cyclohaloalkoxy, (C₂-C₆)alkynyloxy, (C₁-C₆)alkoxy(C₁-C₆)alkyl, (C₃-C₆)cycloalkoxyalkyl, (C₁-C₆)alkoxy(C₃-C₆)cycloalkyl, (C₁-C₆)alkylcarbonyl, (C₃-C₆)cycloalkylcarbonyl, (C₁-C₆)alkoxycarbonyl, (C₄-C₆)alkoxycarbonylalkyl, (C₁-C₆)hydroxyalkyl, substituted or unsubstituted phenyl, phenyl(C₁-C₆)alkyl, heterocyclyl, heterocyclyloxy, heterocyclylcarbonyl, wherein substituents are from one to four and are selected from the group consisting of halo, aminocarbonyl, aminothiocarbonyl, carboxy, formyl, hydroxy, amino, carbamoyl, (C₁-C₃)alkyl, (C₁-C₃)haloalkyl, (C₁-C₃)alkoxy, (C₁-C₃)haloalkoxy, (C₁-C₃)alkylamino, di(C₁-C₃)alkylamino, (C₁-C₂)alkoxy(C₁-C₂)alkyl, (C₁-C₂)alkylamino(C₁-C₂)alkyl, di(C₁-C₂)alkylamino(C₁-C₂)alkyl, (C₁-C₃)alkylcarbonyl, (C₁-C₃)alkoxycarbonyl, (C₁-C₃)alkylaminocarbonyl, and di (C₁-C₃)alkylaminocarbonyl

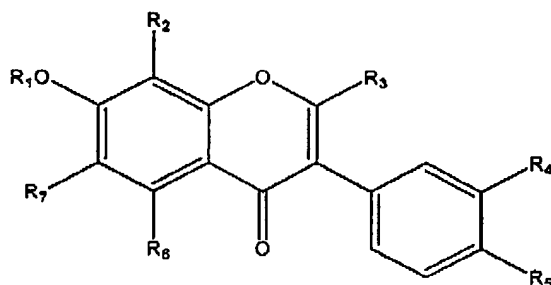
R₆ is selected from the group consisting of hydrogen and hydroxy; and

R₇ is selected from the group consisting of hydrogen, halogen, and C₁-C₆ alkoxy.

3. The method of claim 1, wherein R₅ is hydroxy or amino.
4. The method of claim 2, wherein R₁ is a straight chain alkyl.
5. The method of claim 2, wherein R₁ is (C₁-C₆)hydroxyalkyl or (C₅-C₁₀)carboxyalkyl.
6. The method of claim 1, wherein the ALDH-2 is human ALDH-2.

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7. A method of modulating alcohol consumption in a mammal comprising administering a compound of Formula I



Formula I

wherein:

R₁ is selected from the group consisting of hydrogen, carboxy, halo, branched or straight chain (C₁-C₆)haloalkyl, (C₃-C₆)cycloalkoxy, (C₁-C₆)haloalkoxy, (C₃-C₆)cyclohaloalkoxy, (C₃-C₆)cycloalkoxyalkyl, (C₁-C₆)alkoxy(C₃-C₆)cycloalkyl, (C₃-C₆)cycloalkylcarbonyl, substituted or unsubstituted phenyl, phenyl(C₁-C₆)alkyl, and heterocycloxy, heterocyclylcarbonyl, wherein substituents are from one to four and are selected from the group consisting of halo, aminocarbonyl, aminothiocarbonyl, carboxy, formyl, hydroxy, amino, carbamoyl, (C₁-C₃)alkyl, (C₁-C₃)haloalkyl, (C₁-C₃)alkoxy, (C₁-C₃)haloalkoxy, (C₁-C₃)alkylamino, di(C₁-C₃)alkylamino, (C₁-C₂)alkoxy(C₁-C₂)alkyl, (C₁-C₂)alkylamino(C₁-C₂)alkyl, di(C₁-C₂)alkylamino(C₁-C₂)alkyl, (C₁-C₃)alkylcarbonyl, (C₁-C₃)alkoxycarbonyl, (C₁-C₃)alkylaminocarbonyl, and di (C₁-C₃)alkylaminocarbonyl;

R₂ is selected from the group consisting of hydrogen and alkoxy;

R₃ is selected from the group consisting of hydrogen, (C₁-C₆) alkoxycarbonyl, carboxy and sugar;

R₄ is selected from the group consisting of hydrogen and hydroxy;

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R₅ is selected from the group consisting of hydrogen, carboxy, hydroxy, amino, halo, branched or straight chain (C₁-C₆)alkyl, (C₁-C₆)haloalkyl, (C₂-C₆)alkenyl, (C₃-C₆)alkadienyl, (C₁-C₆)alkoxy, (C₃-C₆)cycloalkoxy, (C₁-C₆)haloalkoxy, (C₃-C₆)cyclohaloalkoxy, (C₂-C₆)alkynyloxy, (C₁-C₆)alkoxy(C₁-C₆)alkyl, (C₃-C₆)cycloalkoxyalkyl, (C₁-C₆)alkoxy(C₃-C₆)cycloalkyl, (C₁-C₆)alkylcarbonyl, (C₃-C₆)cycloalkylcarbonyl, (C₁-C₆)alkoxycarbonyl, (C₄-C₆)alkoxycarbonylalkyl, (C₁-C₆)hydroxyalkyl, substituted or unsubstituted phenyl, phenyl(C₁-C₆)alkyl, heterocyclyl, heterocyclyloxy, heterocyclylcarbonyl, wherein substituents are from one to four and are selected from the group consisting of halo, aminocarbonyl, aminothiocarbonyl, carboxy, formyl, hydroxy, amino, carbamoyl, (C₁-C₃)alkyl, (C₁-C₃)haloalkyl, (C₁-C₃)alkoxy, (C₁-C₃)haloalkoxy, (C₁-C₃)alkylamino, di(C₁-C₃)alkylamino, (C₁-C₂)alkoxy(C₁-C₂)alkyl, (C₁-C₂)alkylamino(C₁-C₂)alkyl, di(C₁-C₂)alkylamino(C₁-C₂)alkyl, (C₁-C₃)alkylcarbonyl, (C₁-C₃)alkoxycarbonyl, (C₁-C₃)alkylaminocarbonyl, and di (C₁-C₃)alkylaminocarbonyl;

R₆ is selected from the group consisting of hydrogen and hydroxy, and

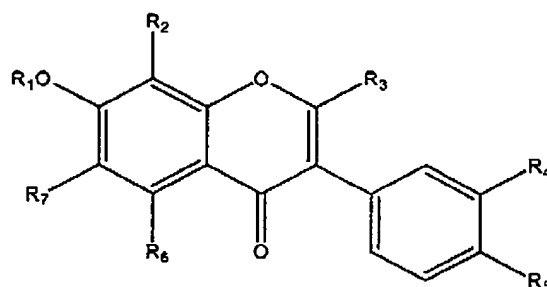
R₇ is selected from the group consisting of hydrogen and halogen,

with the proviso that R₅ cannot be hydroxy when R₁, R₂, R₃, R₄, R₆, and R₇ are all hydrogen

in an amount effective to increase a concentration of an aldehyde formed during catabolism of a neurotransmitter.

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8. A method of modulating alcohol consumption in a mammal comprising administering a compound of Formula I



Formula I

wherein:

R₁ is selected from the group consisting of hydrogen, carboxy, halo, branched or straight chain (C₁-C₆)alkyl, (C₁-C₆)haloalkyl, (C₂-C₆)alkenyl, (C₃-C₆)alkadienyl, (C₁-C₆)alkoxy, (C₃-C₆)cycloalkoxy, (C₁-C₆)haloalkoxy, (C₃-C₆)cyclohaloalkoxy, (C₂-C₆)alkynyloxy, (C₁-C₆)alkoxy(C₁-C₆)alkyl, (C₃-C₆)cycloalkoxyalkyl, (C₁-C₆)alkoxy(C₃-C₆)cycloalkyl, (C₁-C₆)alkylcarbonyl, (C₃-C₆)cycloalkylcarbonyl, (C₁-C₆)alkoxycarbonyl, (C₄-C₆)alkoxycarbonylalkyl, (C₁-C₆)hydroxyalkyl, (C₅-C₁₀)carboxyalkyl, substituted or unsubstituted phenyl, phenyl(C₁-C₆)alkyl, heterocyclyl, heterocyclyloxy, heterocyclylcarbonyl, wherein substituents are from one to four and are selected from the group consisting of halo, aminocarbonyl, aminothiocarbonyl, carboxy, formyl, hydroxy, amino, carbamoyl, (C₁-C₃)alkyl, (C₁-C₃)haloalkyl, (C₁-C₃)alkoxy, (C₁-C₃)haloalkoxy, (C₁-C₃)alkylamino, di(C₁-C₃)alkylamino, (C₁-C₂)alkoxy(C₁-C₂)alkyl, (C₁-C₂)alkylamino(C₁-C₂)alkyl, di(C₁-C₂)alkylamino(C₁-C₂)alkyl, (C₁-C₃)alkylcarbonyl, (C₁-C₃)alkoxycarbonyl, (C₁-C₃)alkylaminocarbonyl, and di(C₁-C₃)alkylaminocarbonyl;

R₂ is selected from the group consisting of hydrogen and alkoxy;

R₃ is selected from the group consisting of hydrogen, (C₁-C₆)alkoxycarbonyl, carboxy and sugar;

R₄ is selected from the group consisting of hydrogen and hydroxy;

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R₅ is selected from the group consisting of hydrogen, carboxy, halo, amino, branched or straight chain (C₁-C₆)alkyl, (C₁-C₆)haloalkyl, (C₂-C₆)alkenyl, (C₃-C₆)alkadienyl, (C₁-C₆)alkoxy, (C₃-C₆)cycloalkoxy, (C₁-C₆)haloalkoxy, (C₃-C₆)cyclohaloalkoxy, (C₂-C₆)alkynyloxy, (C₁-C₆)alkoxy(C₁-C₆)alkyl, (C₃-C₆)cycloalkoxyalkyl, (C₁-C₆)alkoxy(C₃-C₆)cycloalkyl, (C₁-C₆)alkylcarbonyl, (C₃-C₆)cycloalkylcarbonyl, (C₁-C₆)alkoxycarbonyl, (C₄-C₆)alkoxycarbonylalkyl, (C₁-C₆)hydroxyalkyl, substituted or unsubstituted phenyl, phenyl(C₁-C₆)alkyl, heterocyclyl, heterocyclyloxy, heterocyclylcarbonyl, wherein substituents are from one to four and are selected from the group consisting of halo, aminocarbonyl, aminothiocarbonyl, carboxy, formyl, hydroxy, amino, carbamoyl, (C₁-C₃)alkyl, (C₁-C₃)haloalkyl, (C₁-C₃)alkoxy, (C₁-C₃)haloalkoxy, (C₁-C₃)alkylamino, di(C₁-C₃)alkylamino, (C₁-C₂)alkoxy(C₁-C₂)alkyl, (C₁-C₂)alkylamino(C₁-C₂)alkyl, di(C₁-C₂)alkylamino(C₁-C₂)alkyl, (C₁-C₃)alkylcarbonyl, (C₁-C₃)alkoxycarbonyl, (C₁-C₃)alkylaminocarbonyl, and di (C₁-C₃)alkylaminocarbonyl

R₆ is selected from the group consisting of hydrogen and hydroxy; and

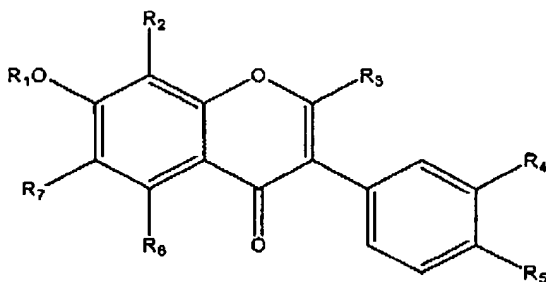
R₇ is selected from the group consisting of hydrogen, halogen, and C₁-C₆ alkoxy,

in an amount effective to increase a concentration of an aldehyde formed during catabolism of a neurotransmitter.

9. The method of claim 7, wherein the mammal is a human.
10. The method of claim 7, wherein the neurotransmitter is serotonin or dopamine.
11. The method of claim 7, wherein the aldehyde is 5-hydroxyindoleacetaldehyde or 3,4-dihydroxyphenylacetaldehyde.

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12. The method of claim 7, wherein the compound does not inhibit monoamine oxidase.
13. The method of claim 7, wherein R_5 is hydroxy or amino.
14. The method of claim 8, wherein R_1 is a straight chain alkyl.
15. The method of claim 8, wherein R_1 is (C_1-C_6) hydroxyalkyl or (C_5-C_{10}) carboxyalkyl.
16. The method of claim 7, wherein the compound is administered intraperitoneally, intramuscularly or orally.
17. A method for identifying a compound that modulates ALDH-2 comprising the steps of:
- i) providing a compound of Formula I



Formula I

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wherein:

R₁ is selected from the group consisting of hydrogen, carboxy, halo, amino, branched or straight chain (C₁-C₆)haloalkyl, (C₃-C₆)cycloalkoxy, (C₁-C₆)haloalkoxy, (C₃-C₆)cyclohaloalkoxy, (C₃-C₆)cycloalkoxyalkyl, (C₁-C₆)alkoxy(C₃-C₆)cycloalkyl, (C₃-C₆)cycloalkylcarbonyl, substituted or unsubstituted phenyl, phenyl(C₁-C₆)alkyl, and heterocyclyloxy, heterocyclylcarbonyl, wherein substituents are from one to four and are selected from the group consisting of halo, aminocarbonyl, aminothiocarbonyl, carboxy, formyl, hydroxy, amino, carbamoyl, (C₁-C₃)alkyl, (C₁-C₃)haloalkyl, (C₁-C₃)alkoxy, (C₁-C₃)haloalkoxy, (C₁-C₃)alkylamino, di(C₁-C₃)alkylamino, (C₁-C₂)alkoxy(C₁-C₂)alkyl, (C₁-C₂)alkylamino(C₁-C₂)alkyl, di(C₁-C₂)alkylamino(C₁-C₂)alkyl, (C₁-C₃)alkylcarbonyl, (C₁-C₃)alkoxycarbonyl, (C₁-C₃)alkylaminocarbonyl, and di (C₁-C₃)alkylaminocarbonyl;

R₂ is selected from the group consisting of hydrogen and alkoxy;

R₃ is selected from the group consisting of hydrogen, (C₁-C₆) alkoxycarbonyl, carboxy and sugar;

R₄ is selected from the group consisting of hydrogen and hydroxy;

R₅ is selected from the group consisting of hydrogen, carboxy, hydroxy, amino, halo, branched or straight chain (C₁-C₆)alkyl, (C₁-C₆)haloalkyl, (C₂-C₆)alkenyl, (C₃-C₆)alkadienyl, (C₁-C₆)alkoxy, (C₃-C₆)cycloalkoxy, (C₁-C₆)haloalkoxy, (C₃-C₆)cyclohaloalkoxy, (C₂-C₆)alkynyloxy, (C₁-C₆)alkoxy(C₁-C₆)alkyl, (C₃-C₆)cycloalkoxyalkyl, (C₁-C₆)alkoxy(C₃-C₆)cycloalkyl, (C₁-C₆)alkylcarbonyl, (C₃-C₆)cycloalkylcarbonyl, (C₁-C₆)alkoxycarbonyl, (C₄-C₆)alkoxycarbonylalkyl, (C₁-C₆)hydroxyalkyl, substituted or unsubstituted phenyl, phenyl(C₁-C₆)alkyl, heterocyclyl, heterocyclyloxy, heterocyclylcarbonyl, wherein substituents are from one to four and are selected from the group consisting of halo, aminocarbonyl, aminothiocarbonyl, carboxy, formyl, hydroxy, amino, carbamoyl, (C₁-C₃)alkyl, (C₁-C₃)haloalkyl, (C₁-C₃)alkoxy, (C₁-C₃)haloalkoxy, (C₁-C₃)alkylamino, di(C₁-C₃)alkylamino, (C₁-C₂)alkoxy(C₁-C₂)alkyl, (C₁-C₂)alkylamino(C₁-C₂)alkyl, di(C₁-C₂)alkylamino(C₁-C₂)alkyl, (C₁-C₃)alkylcarbonyl, (C₁-C₃)alkoxycarbonyl, (C₁-C₃)alkylaminocarbonyl, and di (C₁-C₃)alkylaminocarbonyl;

R₆ is selected from the group consisting of hydrogen and hydroxy; and

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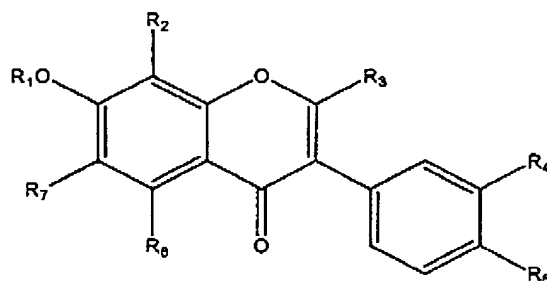
R_7 is selected from the group consisting of hydrogen and halogen, ;

with the proviso that R_5 cannot be hydroxy when R_1 , R_2 , R_3 , R_4 , R_6 , and R_7 are all hydrogen

- ii) contacting ALDH-2 with the compound;
- iii) assaying the ability of the compound to modulate ALDH-2 activity; and
- iv) selecting a compound that modulates ALDH-2 activity as a modulator of ALDH-2 activity.

18. A method for identifying a compound that modulates ALDH-2 comprising the steps of:

- i) providing a compound of Formula I



Formula I

wherein:

R_1 is selected from the group consisting of hydrogen, carboxy, halo, amino, branched or straight chain (C₁-C₆)alkyl, (C₁-C₆)haloalkyl, (C₂-C₆)alkenyl, (C₃-C₆)alkadienyl, (C₁-C₆)alkoxy, (C₃-C₆)cycloalkoxy, (C₁-C₆)haloalkoxy, (C₃-C₆)cyclohaloalkoxy, (C₂-C₆)alkynyloxy, (C₁-C₆)alkoxy(C₁-C₆)alkyl, (C₃-C₆)cycloalkoxyalkyl, (C₁-C₆)alkoxy(C₃-C₆)cycloalkyl, (C₁-C₆)alkylcarbonyl, (C₃-C₆)cycloalkylcarbonyl, (C₁-C₆)alkoxycarbonyl, (C₄-C₆)alkoxycarbonylalkyl, (C₁-C₆)hydroxyalkyl, (C₅-C₁₀)carboxyalkyl, substituted or unsubstituted

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phenyl, phenyl(C₁-C₆)alkyl, heterocyclyl, heterocyclyloxy, heterocyclylcarbonyl, wherein substituents are from one to four and are selected from the group consisting of halo, aminocarbonyl, aminothiocarbonyl, carboxy, formyl, hydroxy, amino, carbamoyl, (C₁-C₃)alkyl, (C₁-C₃)haloalkyl, (C₁-C₃)alkoxy, (C₁-C₃)haloalkoxy, (C₁-C₃)alkylamino, di(C₁-C₃)alkylamino, (C₁-C₂)alkoxy(C₁-C₂)alkyl, (C₁-C₂)alkylamino(C₁-C₂)alkyl, di(C₁-C₂)alkylamino(C₁-C₂)alkyl, (C₁-C₃)alkylcarbonyl, (C₁-C₃)alkoxycarbonyl, (C₁-C₃)alkylaminocarbonyl, and di (C₁-C₃)alkylaminocarbonyl;

R₂ is selected from the group consisting of hydrogen and alkoxy;

R₃ is selected from the group consisting of hydrogen C₁-C₆ alkoxycarbonyl, carboxy and sugar;

R₄ is selected from the group consisting of hydrogen and hydroxy;

R₅ is selected from the group consisting of hydrogen, carboxy, halo, amino, branched or straight chain (C₁-C₆)alkyl, (C₁-C₆)haloalkyl, (C₂-C₆)alkenyl, (C₃-C₆)alkadienyl, (C₁-C₆)alkoxy, (C₃-C₆)cycloalkoxy, (C₁-C₆)haloalkoxy, (C₃-C₆)cyclohaloalkoxy, (C₂-C₆)alkynyloxy, (C₁-C₆)alkoxy(C₁-C₆)alkyl, (C₃-C₆)cycloalkoxyalkyl, (C₁-C₆)alkoxy(C₃-C₆)cycloalkyl, (C₁-C₆)alkylcarbonyl, (C₃-C₆)cycloalkylcarbonyl, (C₁-C₆)alkoxycarbonyl, (C₄-C₆)alkoxycarbonylalkyl, (C₁-C₆)hydroxyalkyl, substituted or unsubstituted phenyl, phenyl(C₁-C₆)alkyl, heterocyclyl, heterocyclyloxy, heterocyclylcarbonyl, wherein substituents are from one to four and are selected from the group consisting of halo, aminocarbonyl, aminothiocarbonyl, carboxy, formyl, hydroxy, amino, carbamoyl, (C₁-C₃)alkyl, (C₁-C₃)haloalkyl, (C₁-C₃)alkoxy, (C₁-C₃)haloalkoxy, (C₁-C₃)alkylamino, di(C₁-C₃)alkylamino, (C₁-C₂)alkoxy(C₁-C₂)alkyl, (C₁-C₂)alkylamino(C₁-C₂)alkyl, di(C₁-C₂)alkylamino(C₁-C₂)alkyl, (C₁-C₃)alkylcarbonyl, (C₁-C₃)alkoxycarbonyl, (C₁-C₃)alkylaminocarbonyl, and di (C₁-C₃)alkylaminocarbonyl

R₆ is selected from the group consisting of hydrogen and hydroxy; and

R₇ is selected from the group consisting of hydrogen, halogen, and C₁-C₆ alkoxy;

ii) contacting ALDH-2 with the compound;

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- iii) assaying the ability of the compound to modulate ALDH-2 activity; and
- iv) selecting a compound that modulates ALDH-2 activity as a modulator of ALDH-2 activity.

19. The method of claim 17, wherein the modulation is inhibition.

20. The method of claim 17, wherein the compound is further capable of increasing a concentration of an aldehyde.

21. The method of claim 20, wherein the aldehyde is 5-hydroxyindoleacetaldehyde or 3,4-dihydroxyphenylacetaldehyde.

22. The method of claim 17, wherein the compound does not inhibit monoamine oxidase.

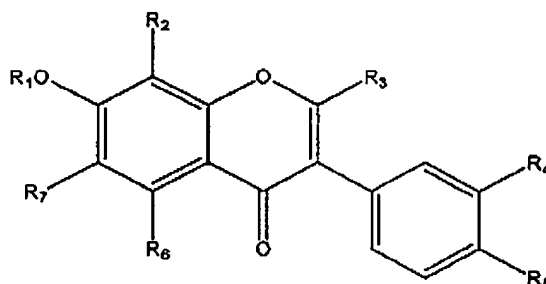
23. The method of claim 17, wherein R_5 is hydroxy or amino.

24. The method of claim 18, wherein R_1 is a straight chain alkyl.

25. The method of claim 18, wherein R_1 is (C_1-C_6) hydroxyalkyl or (C_5-C_{10}) carboxyalkyl.

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26. A compound for inhibiting ALDH-2 comprising Formula I



Formula I

wherein:

R₁ is selected from the group consisting of hydrogen, carboxy, halo, amino, branched or straight chain (C₁-C₆)haloalkyl, (C₃-C₆)cycloalkoxy, (C₁-C₆)haloalkoxy, (C₃-C₆)cyclohaloalkoxy, (C₃-C₆)cycloalkoxyalkyl, (C₁-C₆)alkoxy(C₃-C₆)cycloalkyl, (C₃-C₆)cycloalkylcarbonyl, substituted or unsubstituted phenyl, phenyl(C₁-C₆)alkyl, and heterocycloxy, heterocyclylcarbonyl, wherein substituents are from one to four and are selected from the group consisting of halo, aminocarbonyl, aminothiocarbonyl, carboxy, formyl, hydroxy, amino, carbamoyl, (C₁-C₃)alkyl, (C₁-C₃)haloalkyl, (C₁-C₃)alkoxy, (C₁-C₃)haloalkoxy, (C₁-C₃)alkylamino, di(C₁-C₃)alkylamino, (C₁-C₂)alkoxy(C₁-C₂)alkyl, (C₁-C₂)alkylamino(C₁-C₂)alkyl, di(C₁-C₂)alkylamino(C₁-C₂)alkyl, (C₁-C₃)alkylcarbonyl, (C₁-C₃)alkoxycarbonyl, (C₁-C₃)alkylaminocarbonyl, and di (C₁-C₃)alkylaminocarbonyl;

R₂ is selected from the group consisting of hydrogen and alkoxy;

R₃ is hydrogen;

R₄ is selected from the group consisting of hydrogen and hydroxy;

R₅ is selected from the group consisting of hydrogen, carboxy, hydroxy, halo, amino, branched or straight chain (C₁-C₆)alkyl, (C₁-C₆)haloalkyl, (C₂-C₆)alkenyl, (C₃-C₆)alkadienyl, (C₁-C₆)alkoxy, (C₃-C₆)cycloalkoxy, (C₁-C₆)haloalkoxy, (C₃-C₆)cyclohaloalkoxy, (C₂-C₆)alkynyloxy, (C₁-C₆)alkoxy(C₁-C₆)alkyl, (C₃-C₆)cycloalkoxyalkyl, (C₁-C₆)alkoxy(C₃-C₆)cycloalkyl, (C₁-C₆)alkylcarbonyl, (C₃-C₆)cycloalkylcarbonyl, (C₁-C₆)alkoxycarbonyl, (C₄-

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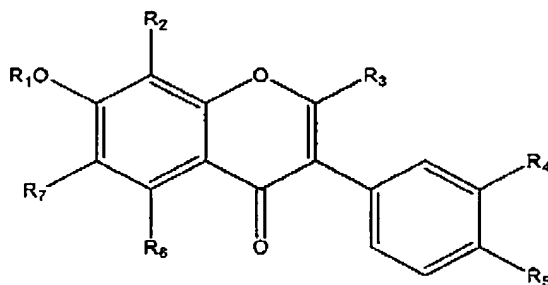
C₆alkoxycarbonylalkyl, (C₁C₆)hydroxyalkyl, substituted or unsubstituted phenyl, phenyl(C₁-C₆)alkyl, heterocyclyl, heterocyclyloxy, heterocyclylcarbonyl, wherein substituents are from one to four and are selected from the group consisting of halo, aminocarbonyl, aminothiocabonyl, carboxy, formyl, hydroxy, amino, carbamoyl, (C₁-C₃)alkyl, (C₁-C₃)haloalkyl, (C₁-C₃)alkoxy, (C₁-C₃)haloalkoxy, (C₁-C₃)alkylamino, di(C₁-C₃)alkylamino, (C₁-C₂)alkoxy(C₁-C₂)alkyl, (C₁-C₂)alkylamino(C₁-C₂)alkyl, di(C₁-C₂)alkylamino(C₁-C₂)alkyl, (C₁-C₃)alkylcarbonyl, (C₁-C₃)alkoxycarbonyl, (C₁-C₃)alkylaminocarbonyl, and di (C₁-C₃)alkylaminocarbonyl;

R₆ is selected from the group consisting of hydrogen and hydroxy; and

R₇ is selected from the group consisting of hydrogen and halogen,

with the proviso that R₅ cannot be hydroxy when R₁, R₂, R₃, R₄, R₆, and R₇ are all hydrogen.

27. A compound for inhibiting ALDH-2 comprising Formula I



Formula I

wherein:

R₁ is selected from the group consisting of hydrogen, carboxy, halo, amino, branched or straight chain (C₁-C₆)alkyl, (C₁-C₆)haloalkyl, (C₂-C₆)alkenyl, (C₃-C₆)alkadienyl, (C₁-C₆)alkoxy, (C₃-C₆)cycloalkoxy, (C₁-C₆)haloalkoxy, (C₃-C₆)cyclohaloalkoxy, (C₂-C₆)alkynyloxy, (C₁-C₆)alkoxy(C₁-C₆)alkyl, (C₃-C₆)cycloalkoxyalkyl, (C₁-C₆)alkoxy(C₃-C₆)cycloalkyl, (C₁-C₆)alkylcarbonyl, (C₃-C₆)cycloalkylcarbonyl, (C₁-C₆)alkoxycarbonyl, (C₄-C₆)alkoxycarbonylalkyl, (C₁-C₆)hydroxyalkyl, (C₅-C₁₀)carboxyalkyl, substituted or unsubstituted

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phenyl, phenyl(C₁-C₆)alkyl, heterocyclyl, heterocyclyloxy, heterocyclylcarbonyl, wherein substituents are from one to four and are selected from the group consisting of halo, aminocarbonyl, aminothiocarbonyl, carboxy, formyl, hydroxy, amino, carbamoyl, (C₁-C₃)alkyl, (C₁-C₃)haloalkyl, (C₁-C₃)alkoxy, (C₁-C₃)haloalkoxy, (C₁-C₃)alkylamino, di(C₁-C₃)alkylamino, (C₁-C₂)alkoxy(C₁-C₂)alkyl, (C₁-C₂)alkylamino(C₁-C₂)alkyl, di(C₁-C₂)alkylamino(C₁-C₂)alkyl, (C₁-C₃)alkylcarbonyl, (C₁-C₃)alkoxycarbonyl, (C₁-C₃)alkylaminocarbonyl, and di (C₁-C₃)alkylaminocarbonyl;

R₂ is selected from the group consisting of hydrogen and alkoxy;

R₃ is hydrogen;

R₄ is selected from the group consisting of hydrogen and hydroxy;

R₅ is selected from the group consisting of hydrogen, carboxy, halo, amino, branched or straight chain (C₁-C₆)alkyl, (C₁-C₆)haloalkyl, (C₂-C₆)alkenyl, (C₃-C₆)alkadienyl, (C₁-C₆)alkoxy, (C₃-C₆)cycloalkoxy, (C₁-C₆)haloalkoxy, (C₃-C₆)cyclohaloalkoxy, (C₂-C₆)alkynyloxy, (C₁-C₆)alkoxy(C₁-C₆)alkyl, (C₃-C₆)cycloalkoxyalkyl, (C₁-C₆)alkoxy(C₃-C₆)cycloalkyl, (C₁-C₆)alkylcarbonyl, (C₃-C₆)cycloalkylcarbonyl, (C₁-C₆)alkoxycarbonyl, (C₄-C₆)alkoxycarbonylalkyl, (C₁-C₆)hydroxyalkyl, substituted or unsubstituted phenyl, phenyl(C₁-C₆)alkyl, heterocyclyl, heterocyclyloxy, heterocyclylcarbonyl, wherein substituents are from one to four and are selected from the group consisting of halo, aminocarbonyl, aminothiocarbonyl, carboxy, formyl, hydroxy, amino, carbamoyl, (C₁-C₃)alkyl, (C₁-C₃)haloalkyl, (C₁-C₃)alkoxy, (C₁-C₃)haloalkoxy, (C₁-C₃)alkylamino, di(C₁-C₃)alkylamino, (C₁-C₂)alkoxy(C₁-C₂)alkyl, (C₁-C₂)alkylamino(C₁-C₂)alkyl, di(C₁-C₂)alkylamino(C₁-C₂)alkyl, (C₁-C₃)alkylcarbonyl, (C₁-C₃)alkoxycarbonyl, (C₁-C₃)alkylaminocarbonyl, and di (C₁-C₃)alkylaminocarbonyl

R₆ is selected from the group consisting of hydrogen and hydroxy; and

R₇ is selected from the group consisting of hydrogen, halogen, and C₁-C₆ alkoxy.

28. The compound of claim 26, wherein R₅ is hydroxy or amino.

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29. The compound of claim 27, wherein R_1 is a straight chain alkyl.
30. The compound of claim 27, wherein R_1 is (C_1-C_6) hydroxyalkyl or (C_5-C_{10}) carboxyalkyl.
31. The compound of claim 26, wherein the compound further inhibits alcohol consumption in a mammal.
32. The compound of claim 31, wherein the mammal is a human.

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